REMARKS

Claims 46-72 were pending in the application, prior to the present amendment, in which claims 54 and 70 have been canceled. Claims 62-72 have been withdrawn from consideration, pursuant to a Restriction Requirement, which has been made final, leaving claims 46-61 subject to examination.

Claims 46-51 were provisionally rejected under the judicially-created Doctrine of Obviousness-Type Double Patenting; claims 46-51 and 56-61 were rejected under 35 U.S.C. § 102(b); claims 46-61 were rejected under 35 U.S.C. § 102(e); and claims 46-61 were rejected under 35 U.S.C. § 103(a).

The Restriction Requirement and each of the rejections are addressed below.

First, Applicants submit that, in the interest of expediting prosecution, the claims have been amended to denote very specific peptides. In particular, the peptides of the present claims each include the sequence of SEQ ID NO:13 (KLVF), in which each amino acid of this sequence is a [D]-amino acid. Peptides with this particular requirement are not described in the prior art and Applicants respectfully submit that claims specifying such peptides are thus novel and also are non-obvious over the prior art. Applicants further submit that the claims have also been amended to specify that adjuvants are used or included in the claimed methods and compositions. Support for this amendment can be found, for example, in canceled claims 54 and 70. No new matter has been added by the present amendments.

Restriction Requirement

Applicants maintain their traversal of the Restriction Requirement. As was noted in the Reply to Restriction Requirement, filed on April 20, 2006, Applicants respectfully submit that all of the present claims should be considered to fall within a single group for the purposes of Restriction analysis, as claims 46-61 specify methods of use of a particular vaccine, and claims 62-72 specify that particular vaccine itself. Thus, the inventions of these claims are related products and processes, wherein the vaccines are used in the vaccination methods, and the vaccination methods employ the vaccines. In view of the close relationship between the claimed methods and vaccines, Applicants submit that the claims of Groups I and II should be examined together.

In making the Restriction Requirement final, the Examiner comments that the inventions of Groups I and II can be shown to be distinct (and thus subject to restriction) if "(1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product." In applying these standards to the present case, the Examiner states that the method claims of Group I "could be practiced instead with a materially different product, for example with an Aβ antibody, and still achieve the desired result of treating a subject by altering levels of amyloid-β in the brain of the subject." In response, Applicants note that the claims of Group I specify the use of a vaccine including a particular peptide, and not antibodies, as noted by the Examiner. Thus, this basis for maintaining the Restriction Requirement should be withdrawn.

The Examiner further states "the vaccine comprising the amyloid-β peptide could be used to recover existing anti-Aβ antibodies from a patient sample, such as in affinity chromatography,

and thus could be used in diagnostic testing." In response, Applicants note that the claimed vaccine compositions are just that: vaccine compositions. If used for the purposes noted by the Examiner, the compositions would not be vaccines. Applicants further submit that, as is noted above, the present claims have been amended to specify that the claimed vaccines include an adjuvant. Such compositions would be used for vaccination, and not for the purposes noted by the Examiner. Applicants thus request that this basis for maintaining the Restriction Requirement be withdrawn.

Finally, the Examiner notes that the search for the vaccine would not be informative as to the novelty or non-obviousness of the methods, the searches would not be co-extensive, and that they would thus be very burdensome. Applicants respectfully request that the Examiner reconsider this matter. In particular, a search for both groups of claims could center on a search of the sequence that is common to each group, with the results being analyzed with respect to the claims of each group, in the absence of an undue burden. Further, because the composition claims specify a vaccine, and the method claims specify vaccination, it would seem that analysis with respect to Groups I and II would at least substantially overlap. Applicants thus request reconsideration of the Restriction Requirement.

Double Patenting

Claims 46-51 were provisionally rejected under the judicially-created Doctrine of Obviousness-Type Double Patenting over claims 1, 4, 8, and 10 of U.S. Serial No. 10/895,646. When the only rejection remaining in a case is a provisional double patenting rejection, an application should be allowed to issue. M.P.E.P. § 822.01. In view of the amendments and

remarks provided herein, Applicants submit that all of the grounds of rejection in this case, other than the provisional double patenting rejection, have been met. Accordingly, the provisional double patenting rejection should be withdrawn and the case allowed to issue.

Rejections under 35 U.S.C. § 102

Claims 46-51 and 56-61 were rejected under 35 U.S.C. § 102(b) as being anticipated by Findeis et al., WO 96/28471. The Examiner states that Findeis teaches the administration of compounds such as those of the present claims for the treatment of amyloidosis disorders, such as Alzheimer's disease and hereditary cerebral hemorrhage (a type of cerebral amyloid angiopathy), as well as the modulation of aggregation and neurotoxicity of β-amyloid peptides. With respect to induction of an immune response, the Examiner states that "although Findeis does not explicitly state that these compounds elicit an immune response in a subject, the skilled artisan would recognize that the act of administering the Aβ-derived compounds, which are identical to the peptide vaccine instantly claimed, would intrinsically result in the production of anti-amyloidogenic antibodies..." and that "such anti-amyloidogenic antibodies would inherently alter levels of soluble amyloid-β as well as prevent fibrillogenesis in the brains of those subjects to whom the immunogenic peptides were administered." Applicants respectfully request that this rejection be withdrawn, for the following reasons.

First, Applicants note that, in the interest of expediting prosecution, the present claims have been amended to specify the presence and use of an adjuvant in the claimed compositions and methods. The concept of vaccination, and thus the use of adjuvants, is nowhere present in the Findeis patent, which thus does not anticipate the present claims. In the interest of

completion, Applicants note that, even without specifying the use of an adjuvant, the methods of the present claims are different from those of Findeis. For example, as is noted above, the present claims now specify the use of peptides in which the sequence of SEQ ID NO:13 is in all-D form, which is not mentioned by Findeis. Also, Findeis does not teach vaccines or vaccination methods.

Claims 46-61 were rejected as being anticipated by Schenk, U.S. Patent No. 6,743,427, in view of Kalaria, Ann. N.Y. Acad. Sci. 893:113-125, 1999. Schenk is cited for teaching β-amyloid peptides and fragments, in conjunction with an adjuvant and/or coupled to a carrier protein, for use in inducing an immune response in a host to which they are administered. The Examiner notes that one peptide noted by Schenk is SEQ ID NO:21 (HHQKLVFFAE), which is the same as SEQ ID NO:27 of the present application, and thus would also encompass SEQ ID NO:13 (KLVF), as is specified in the present claims. With respect to [D]-amino acids, the Examiner notes that "Schenk teaches that analogs of the Aβ peptides include unnatural amino acids, such as D-amino acids, as well as modifications of N or C terminal amino acids at one, two, or a few positions (see column 11, lines 24-29)." Kalaria is cited to show that treatment of Alzheimer's disease would include the treatment of cerebral amyloid angiopathy. Applicants submit that this rejection should be withdrawn.

As is noted above, the present claims specify peptides that comprise an amino acid sequence as set forth in SEQ ID NO:13, wherein at least the portion corresponding to SEQ ID NO:13 consists entirely of [D]-amino acids. Schenk does not teach such peptides or their use. Rather, the teaching of Schenk is more general and does not provide any specificity as to the presence of [D]-amino acids in any particular positions, not to mention those of the very specific

sequence of SEQ ID NO:13 (KLVF). This rejection should therefore be withdrawn, as Schenk does not teach the peptides of the present claims. (Kalaria also does not teach such peptides.)

Rejections under 35 U.S.C. § 103(a)

Claims 52-55 were rejected for obviousness over Findeis, WO 96/28471, in view of Schenk, WO 99/27944. Findeis is cited for teaching administration of compounds including Aβ sequences such as KLVFFA and KLVFF, which encompass SEQ ID NO:13 of the present claims, for treating amyloidosis. Findeis is also cited for teaching that such compounds can be modified by substituting all-D amino acids for all-L amino acids. The Examiner notes that Findeis does not teach administration of such compounds with adjuvants or carrier molecules. However, the Examiner cites Schenk for teaching the administration of Aβ peptides, in association with a carrier or in combination with an adjuvant, for the induction of an immune response. In combining the teachings of these references to support the present rejection, the Examiner states "it would have been obvious to combine the method of modulating the aggregation of amyloidogenic proteins by administering Aβ peptides in conjunction with an adjuvant or carrier protein in order to enhance the immune response to the peptide immunogens. The artisan would be motivated to produce anti-amyloidogenic, immunogenic peptides comprising KLVF (SEQ ID NO:13) in all D-amino acid conformation coupled to a carrier or administered with an adjuvant, to provide treatment of amyloidogenic diseases as recognized in the art via not only their anti-fibrillogenic properties, but also for their immunogenic property..." Applicants respectfully disagree.

In particular, in making this rejection, the Examiner combines references describing two opposing technologies: (i) the use of antifibrillogenic peptides binding to Aβ and inhibiting fibril formation (Findeis), and (ii) the use of peptides to induce an immune response against Aβ (Schenk), and suggests that it would have been obvious to use the former approach in conjunction with the latter. Applicants respectfully disagree, because these approaches involve two totally different mechanisms, and those skilled in the art would not have been motivated to combine them. Indeed, if peptides such as those of Findeis were to be used as vaccines (due to the presence of an adjuvant), those peptides would have to stimulate the production of antibodies against them to be effective, and those antibodies would thus bind to the Aβ proteins/peptides and thus prevent any antifibrillogenic activity that the peptides could have. Thus, those skilled in the art would either use the peptides as antifibrillogenic agents or as vaccine antigens, but not as agents having both activities, as suggested by the Examiner. Because of these fundamental differences in the approaches of Findeis and Schenk, which indeed are opposing and contradictory, these references cannot be combined to support an obviousness rejection of the present claims. Applicants thus request that this rejection be withdrawn.

Claims 46-61 were rejected for obviousness over Schenk, WO 99/27944; Alberts et al., Molecular Biology of the Cell, 2nd Edition, 1989; and Kalaria et al., Ann. N.Y. Acad. Sci. 893:113-125, 1999; in view of Tjernberg et al., J. Biol. Chem. 271:8545-8548, 1996; Findeis, WO 96/28471; Van Regenmortel et al., Curr. Opin. Biotech. 9:377-382, 1998; Isowa et al., U.S. Patent No. 4,116,768; and Clayberger et al., U.S. Patent No. 6,436,903. This rejection is respectfully traversed.

Schenk is cited for teaching the administration of Aβ peptides for the induction of an

immune response. The Examiner notes, however, that Schenk does not teach Aβ peptides that consist entirely of [D]-amino acids, or peptides including particular amino or carboxyl terminal substituents or amino acid substitutions.

Tjernberg and Findeis are cited for teaching Aβ peptides and their use in preventing amyloid fibril formation, with Findeis also being cited for teaching substitutions of all D-amino acids for all L-amino acids in such peptides. Van Regenmortel is cited for teaching that peptides assembled from D-amino acids are more stable to proteolysis than L-peptides, Isowa is cited for teaching the use of amino and carboxyl terminal protective groups for the stabilization of peptide compounds, and Clayberger is cited for teaching immunomodulating peptide compounds including D-amino acids, N-terminal acylated and C-terminal amidated peptides, and the use of modified amino acids such as, for example, phenylglycine. Based on these references, the Examiner states that those of skill in the art "would be motivated to produce anti-amyloidogenic immunogenic peptides comprising KLVF (SEQ ID NO:13) in all D-amino acid conformation, with or without N- or C-terminal protective groups, with or without conservative amino acid substitutions... and coupled to a carrier or administered with an adjuvant, to provide treatment of Alzheimer's disease (and cerebral amyloid angiopathy) as recognized in the art via both its immunogenic and anti-fibrillogenic properties." Applicants respectfully disagree.

As is stated above in reference to the rejection over the combination of Findeis and Schenk, approaches involving inhibition of fibril formation by peptides and use of peptides as vaccine antigens involve completely different, and indeed contradictory mechanisms. Because of this, those of skill in the art would not have been motivated to combine these approaches. Similar to what is stated above in connection with the prior rejection, if peptides such as those of

Findeis or Tjernberg were to be used as vaccines, they would stimulate the production of antibodies against them, and the antibodies would bind to the administered Aβ peptides and thus prevent their antifibrillogenic activity. Thus, those skilled in the art would recognize that the Aβ peptides can be used either as antifibrillogenic agents or as vaccine antigens, but not as agents having both activities, as stated by the Examiner. Because of these very fundamental, opposing, and contradictory differences, references describing these different approaches cannot be properly combined to support an obviousness rejection of the present claims.

The references describing, e.g., increased stability of peptides including [D]-amino acids, terminal modifications, and/or conservative substitutions do not provide any information that overcomes this fundamental problem with this rejection, which Applicants thus request be withdrawn.

Applicants further note that, as indicated by the Examiner at page 16, second paragraph, of the Office Action, Schenk does not teach the claimed sequences consisting entirely of [D]-amino acids. The same is true for the other references cited in this rejection. Thus, the claimed immunogenic peptides, which include the sequence of SEQ ID NO:13 made exclusively of [D]-amino acids, are an unexpected selection over the various peptides fragments suggested by Schenk and others. As discussed above, the present claims now focus on very specific, novel, and non-obvious peptides. This rejection should therefore be withdrawn.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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